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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,608	03/24/2004	Bahram Ghaffarzadeh Kermani	01-00011	7232
29389	7590	06/03/2005	EXAMINER	
ILLUMINA, INC. 9885 TOWNE CENTRE DRIVE SAN DIEGO, CA 92121-1975			ZHOU, SHUBO	
			ART UNIT	PAPER NUMBER

1631

DATE MAILED: 06/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

10/809,608

Applicant(s)

KERMANI, BAHRAM
GHAFFARZADEH

Examiner

Shubo (Joe) Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-11, 13-29 and 47-89 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-11, 13-29 and 47-89 is/are rejected.
- 7) ☒ Claim(s) 9-11, 13, 17, 18, 20, 21 and 23-27 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicants' amendment and request for reconsideration in the communication filed on 3/23/05, is acknowledged and the amendments entered. Claims 1-4, 6-11, 13-29, 47-48, and newly added claims 49-89 are currently pending and under consideration.
2. Applicant's arguments in response to the previous Office action have been fully considered but they are not deemed to be persuasive. The following rejections and/or objections are either reiterated from the previous Office action mailed 3/10/05 or newly applied, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Specification

3. The specification is objected to because of the following:

It appears that trademark is used in this application, such as BEADARRAYTM (registered by Illumina, Inc., 9390 Towne Center Drive, Suite 200, San Diego, CALIFORNIA 92121) on page 11. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The specification is objected to also because the Brief Description of the Drawings at page 4 fails to correspond to the actual drawing. The specification refers to Figure 8, but the Drawings filed 7/12/04 do not have Figure 8, but Figure 8A, Figure 8B, etc.

Appropriate correction is required.

Claim Rejections-35 USC § 112

4. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 28-29 and 88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28 and 29 are amended to contain “a balancing signal transformation,” for which applicants assert that the specification provides support on page 22, line 29 through page 23, line 7. However, the portion of the specification referred to by applicants only discuss various methods of signal transformation, not “a balancing signal transformation.” Such “a balancing signal transformation” is not found disclosed in the specification. Newly added claim 88 contains a step of balancing by signal transformation, which is also not described in the specification in

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such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 47-89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47, as well as its dependent claims 49-69, appears to be drawn to a genotyping system in the preamble. However, none of the components (a) through (d) of the system is clearly indicated to be used to accomplish such a task for the system. Thus, it is unclear whether such components for genotyping are required in the system. The metes and bounds of the claimed invention are thus not clear.

Similarly, claim 48, as well as its dependent claims 70-89, appears to be drawn to a method of determining a genotype score in the preamble. However, none of the steps (a) through (i) of the method is clearly indicated to accomplish such a task for the method. Thus, it is unclear whether such step for determining a genotype score is required in the system. The metes and bounds of the claimed invention are thus not clear.

Clarification of the metes and bounds of the claims is requested.

Claim Rejections-35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, 6-8, 19 and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hill et al. (Genome Biology, Vol. 2, No. 12, pages 1-13, 2001).

This rejection is reiterated from the previous Office action.

Hill et al. disclose different methods of normalizing microarray data including constant mean normalization and frequency normalization. The microarray data comprise expression data for genes from oocytes or two-week old worms. See page 10, right column, last paragraph. It would be readily recognized by one of ordinary skill in the art that the two-week old worms referred to by Hill et al. would be diploid. Therefore, the genome of the worms used for the experiment comprises two alleles of every locus. Further, the array (such as the A array referred to on page 10) comprises sets of probes, and each set consists of 20 distinct probe pairs designed to monitor one single transcript. Thus, the 20 different probes are designed to detect different alleles of a single locus. See page 10, right column. Since the microarray is performed using total RNA as target nucleic acids isolated from the worms, it would be recognized by one of skill in the art that the expression data would comprise the different signals of the two alleles of any locus, which reads on the first and second allele recited in the claims (see also page 11, lines 1-2). The expression data are presented in a Cartesian coordinate system. See Figures 1 and 2. This reads on the limitations of step (a) of claim 1. Hill et al. disclose a normalization method referred to as frequency normalization. Hill et al. state (see page 4, left column, last paragraph, and the right column, Figure 2):

“The specific hybridization intensity (AD) value for each of the 11 spike-in controls is plotted as a function of transcripts frequency in units of transcripts per million. The points are fitted with a generalized linear model that is then used as a calibration curve to compute frequencies from the AD values of the other genes on the array.”

Those points that are on the solid fitted line in Figure 2 are interpreted to read on the sweep points as recited in step (b) of claim 1 because sweep points are defined as “a set of points that are spaced according to a defined function along a line or curve” (page 7 of the specification). Those points that are not on the fitted line but close to the line are interpreted to read on the control points as recited in step (c) of claim 1 because they are for calibration and normalization as a control point is defined as “a signal value upon which normalization is based.” See also page 7 of the specification.

Hill et al. disclose that using the fitting curve, chip sensitive as a parameter is determined as shown by the vertical line in Figure 2. All the other signal values of other genes on the array are calibrated and thus transformed based on the curve. These reads on steps (d) and (e).

As to claim 2-4, Hill et al. disclose some of the genetic data in a graphical format such as those in Figures 1, 2, which are Cartesian coordinates, and some in tabular format such as those in Tables 1-2. The probe sets on the arrays used by Hill et al. comprise thousands of genes. See page 10, right column.

As to claims 6-8, Hill et al. disclose that a mild curvature is noticed when a power law model is fitted to the data in Figure 2 indicating that there is a saturation, and use of 1 microgram cRNA would eliminate the saturation. This reads on the limitation of “upper limit” of claim 7. Figure 2 also shows the cutoff line for the limit of detection (the vertical line). This reads on the limitation of “lower limit” in claim 8.

As to claim 19, as set forth above, the sweep points are located on a line in Figure 2.

As to claim 22, the coordinate system disclosed by Hill et al. in Figure 2 comprises two dimensions, i.e. the axes X and Y.

Applicant's arguments filed 3/25/05 have been fully considered but they are not persuasive.

Applicants argue that since claim 1 is amended to contain a step of "projecting said control points to a line or curvature passing through said sweep points, thereby forming set points," thus the claims are now not anticipated by Hill et al. This is not persuasive because Hill et al. do disclose such a limitation. As set forth above, Hill et al. in Figure 2, project a line that goes through the sweep points. Any points on the line read on the "set points" recited in the claim.

10. Claims 14-16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hill et al. (Genome Biology, Vol. 2, No. 12, pages 1-13, 2001).

Claims 14-16 are amended to be dependent from claim 1.

As applied to claims 1-4, 6-8, 19 and 22 above, Hill et al. disclose a method for normalizing genetic data that reads on the invention of the claims. See the above section for details.

As to claims 14-16, as cited above, Hill et al. on page 4 and Figure 2 clearly indicate that "the points are fitted with a generalized linear model that is then used as a calibration curve." As set forth above, these points on the line of Figure 2 read on the "control points" of the claims. Since any points on the line are considered as reading on the set points of the claims, the control points are projected onto the set points. As to the polynomial transformation recited in claim 16, while the legend for Figure 2 does not explicitly state that the AD is plotted through a

polynomial transformation, the formula, a polynomial formula, on page 12 for projecting AD clearly indicates that the AD on Figure 2 is plotted and projected using the same formula.

This rejection is newly applied and is necessitated by the amendments to the claims.

Claim Objections

11. Claims 9-11, 13, 17-18, 20-21, and 23-27 are objected to as being dependent upon a rejected base claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the

advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

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Shubo (Joe) Zhou, Ph.D.



Patent Examiner

 5/31/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER